

Scientific Abstract

We propose initiation of a Phase I dose escalation study on Intra-articular pNGVL-TK plasmid DNA followed by systemic ganciclovir (hereafter referred to as TK/GCV) for the treatment of active rheumatoid synovitis of the knee. We propose to study 4 doses of pNGVL-TK plasmid DNA over a range of one and one-half logs (0.3 mg, 3.3 mg, 10.0 mg). A constant dose of intravenous ganciclovir (5 mg/kg twice daily for three days) will be used for each dose of pNGVL-TK plasmid DNA tested. We propose to study 2 patients at each dose of pNGVL-TK plasmid DNA, a total of 8 patients.

The three major goals of this Phase I trial are; 1) to establish that rheumatoid synoviocytes can be transfected in vivo using intra-articular administration of naked pNGVL-TK plasmid DNA, 2) to establish the safety of the plasmid based TK/GCV intra-articular treatment, and 3) to identify biological effects specific to the TK/GCV gene therapy. In order to achieve these goals, we believe that arthroscopically guided synovial biopsy of the knee is the best clinical procedure available for the acquisition of synovial tissues for necessary histologic and molecular analyses. We believe that clinical examination combined with power Doppler sonography represent the best non-invasive methods available to monitor clinical effects associated with the TK/GCV gene therapy over an extended period of observation.